

REMARKS

Claims 1-6 are pending and await further action on the merits.

[II] Issues under 35 U.S.C. § 102(b)

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kaspersen et al. (Journal of Label. Comp. and Radiopharm., 27, No. 9, 1055, 1989). The Examiner has maintained the rejection of claims 1-5 and has included new claim 6 in the rejection. Applicants respectfully traverse the rejection.

[I-A] Instant claims 5-6

Applicants now comment on the patentability of the inventions described in instant claims 5-6.

In the outstanding Office Action, the Examiner has commented on the melting point discrepancy between the mirtazapine crystal of Kaspersen et al. and the melting point described in claims 5 and 6. Specifically, instant claims 5 and 6 recite that the melting point of the crystals is 114-116 °C whereas Kaspersen et al. teach that the mirtazapine product has a melting point of 123.8-125.8 °C. The Examiner notes this difference but has stated that the “melting difference could arise from impurities in the product. It could also arise from human error or instrumentation error.”

Applicants respectfully disagree with the Examiner's comments. First, Applicants agree with the Examiner that a melting point can change when impurities are present in the crystalline structure. However, claims 5 and 6 exclude these impurities by reciting the melting point range of 114-116 °C which is sharp and differs from the melting point range of Kaspersen et al by at least 7.8°C (123.8-116).

Second, with respect to the Examiner' assertion that the difference in the melting point could be from human error or instrumentation error, it is Applicants' position that the Examiner must take the description of Kaspersen et al. as being true unless there is some other valid reason

to suspect that the description is false. The article to Kaspersen et al. made it through peer review and appears in a respected journal, i.e., the Journal of Labelled Compounds and Radiopharmaceuticals.

Furthermore, this line of reasoning used by the Examiner is a slippery slope which is frowned upon by the patent office. MPEP 2121 states that a prior art reference is presumed to be operable and enabling. The burden is on Applicants to show otherwise. Here the Examiner appears to be putting the burden on Applicants to prove that the reference is operable, i.e., that the melting point is actually 123.8-125.8 °C as described by Kaspersen et al. However, the Examiner has provided no valid reason why Kaspersen et al. were able to make it through peer review with incorrect information. As such, there is a clear distinction between the teachings of Kaspersen et al. and the invention as described in instant claims 5-6. Accordingly, withdrawal of the rejection to the extent that it applies to claims 5-6 is respectfully requested.

[I-B] Instant claims 1-4

With respect to instant claims 1-4, the Examiner has not addressed all of the arguments for patentability which have been made of record by Applicants. As such, Applicants herein reiterate the arguments for patentability which are of record.

The Examiner has maintained the position that Applicants are required to repeat the experiments of Kaspersen et al. to show that the mirtazapine crystals of Kaspersen et al. do not have (i) a water content of not more than 0.5% by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, as presently claimed.

The Examiner has agreed in the August 28, 2006 Interview that the process of Kaspersen et al. uses "ordinary drying conditions" as is described in Example 8 in the present specification.

It is Applicants' position that Example 8 in the present specification is sufficiently close to the description of Kaspersen et al., so that the skilled artisan would come to the reasonable conclusion that the mirtazapine crystals of Kaspersen et al. do not have (i) a water content of not

more than 0.5% by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, as presently claimed.

The workup of Kaspersen et al. is as follows:

The product was extracted with ethyl acetate, dried over Na₂SO₄ and evaporated to dryness to yield 950 mg (85%) of crude 1c. The crude 1c was purified by chromatography over Alox B (eluted with hexane/ethyl acetate 7:3, v/v) to yield 830 mg. For the final purification the product was treated twice with 100 mg of charcoal in n-hexane (containing 1% of methanol) followed by crystallization from methanol/water (1:1, v/v) yielding 600 mg (53%) Org 3770 as colourless crystals, m.p. 123,8-125,8 °C. No impurities were detectable either on TLC, HPLC or GC.

The Examiner will note that Example 8 of the present application and the invention of Kaspersen et al. are the same in that mirtazapine is recrystallized from a solvent mixture of methanol/water. Also, the Examiner will note that the mirtazapine of Example 8 was dried under ordinary conditions. In view of these similarities, it is appropriate for the Examiner to rely on the experimental data of Example 8 in the present specification to show the properties of the final mirtazapine crystals of Kaspersen et al., and for the Examiner to rely on the experimental data of Example 7 in the present specification to show the properties of the final mirtazapine crystals of the present invention which are dried under relatively stringent conditions.

The product of Example 8 has a water content of about 3.5 % by weight, which is outside the inventive range of water content of "not more than 0.5% by weight". Since the product of Kaspersen et al. is also dried under ordinary conditions, it follows that the product of Kaspersen et al. has a water content of about 3.5 % by weight. Thus, Example 8 of the present specification is relevant to show that it is likely that the product of Kaspersen et al. is outside the inventive range of water content of "not more than 0.5% by weight".

Based on the foregoing, withdrawal of the rejection is respectfully requested.


In view of the above amendment, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Garth M. Dahlen, Ph.D., Esq. Reg. No. 43,575 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: January 18, 2007

Respectfully submitted,

By  43575
Gerald M. Murphy, Jr. 80✓
Registration No.: 28,977
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant